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Atty Docket No. 656.0005 PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In application of: Stewart et al

NOUJAIM, et al. Group Art Unit: 1643 → 1644

Serial No.: 09/438,944

Filed: November 12, 1999 Examiner: DECLOUX, A.

For: COMPOSITIONS AND METHODS FOR PRODUCING VASCULAR OCCLUSION

APPELLANT'S BRIEF ON APPEAL

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APPELLANTS' BRIEF ON APPEAL

1. Real Party In Interest

Applicants and their company, ViRexx Research, Inc., are the parties in interest.

2. Related Appeals

Not applicable.

3. Status Of Claims

(1) Claims 12, 14, 17, 18, and 29-39 are currently pending in this application and are the claims involved in this Appeal. See Appendix A.

(2) Claims 1-11, 13, 15-16, 19-28 were canceled previously and not to be considered as part of this appeal.

4. Status Of Amendments

An Amendment after Final was filed on June 20, 2002. In an Advisory Action mailed July 17, 2002, the Amendment filed June 20, 2002 was not entered because the amendment raises new issues and because the amendment is not deemed to have placed the application in better form for appeal.

5. Summary Of The Invention

The invention is a method for producing a vascular occlusion (e.g., a thrombus) by immobilizing von Willebrand Factor (vWF) at a target site (e.g., a tumor site), and using the natural function of the vWF to bind and activate platelets, which in turn causes the a thrombus to form (page 1, lines 16-19). The invention relies on the natural function of vWF to bind and activate platelets (page 2, line 15 to page 3, line 5). The invention further relies on the natural function of platelets, when activated, to form a thrombus (page 3, lines 6-21).

The technology of the present invention mimics the cell-based, physiologic response to vascular damage. Specifically, immobilizing VWF to a target site leads to platelet deposition, even in the absence of the coagulation protein cascade. Example 8 demonstrates that platelets were found to localize, activate and aggregate at a target site even when the coagulation protein cascade was inhibited (i.e. anti-coagulated blood). Including a human Fc component to the targeting agent was shown to enhance the rate and extent of platelet activation and aggregation about the target site. This Fc component specifically increased platelet activation in synergy with the immobilized VWF (solid-phase

platelet binder) by engaging a receptor on the surface of the platelet, in the absence of a functioning coagulation cascade. However, in the absence of the cellular components of blood (specifically platelets), immobilization of VWF to a target site did not produce a thrombus, nor did the immobilized VWF activate the coagulation protein cascade.

The novelties of the present invention include, (i) specific localization of a cell (platelets) to a target site using an immobilized platelet binder, and (ii) a platelet-dependent initiation of thrombus generation versus a coagulation protein-dependent initiation of a thrombus.

In all of its steps, the method of the present invention includes:

1. Site is targeted (e.g., in proximity to tumor, or tumor cell itself, or pre-determined molecule)
2. Targeting moiety also binds vWF
3. vWF captured at site
4. vWF captures unactivated platelets
5. Platelets activate
6. Platelets aggregate, mediated by vWF and soluble fibrinogen
7. Platelet plug formed, clot formed

Of these various steps, the use of immobilized vWF to capture and activate platelets is novel. The other steps – targeting a site, the elements for binding vWF, vWF capturing platelets and activating them, platelet aggregation, and thrombus formation – all are either well known constructs or processes, or are well known and well described natural processes. The technology of the present invention follows the chronological sequence of the normal hemostatic response, whereby circulating platelets contact and bind to exposed subendothelium activate and aggregate thereby forming a platelet plug that prevents further blood loss from the damaged blood vessel (refer to Ruggeri, 2000).

6. Issues

(1) Whether claims 12, 14, 17, 18, and 29-39 are definite under 35 U.S.C. 112, second paragraph.

(2) Whether claims 12, 14, 17, 18, and 29-39 are enabled under 35 U.S.C.

112, first paragraph.

(3) Whether claims 12, 14, 17, 18, and 29-39 were in possession of the inventors under 35 U.S.C. 112, first paragraph.

(4) Other informality and procedural considerations.

7. Grouping Of Claims

For purposes of this Appeal only, Appellant groups the claims as follows: Claim 12 stands alone, and claims 14, 17, 18, and 29-39 stand and fall together.

8. Argument

Prior to discussing each rejection, Appellant believes the Examiners assertion of informalities on Issues 2 and 3 are improper rejections based on an improper application of the law, based on unsound and/or inconsistent reasoning, and/or based on unsupported assertions. To properly reject the claims, the Examiner can not require the inclusion of known elements into the claims, and the asserted arguments must be supported by sound reasoning or an independent reference. Further, Applicants have been open and forthcoming with the Examiner regarding Applicants start-up company's commercial needs to streamline the prosecution of this application, and so Applicants have a co-pending application in which "problem" issues are being addressed, and Applicants have readily complied with all oral and written requests by the Examiner. Indeed, the Examiner and her supervisor acknowledged in our interview of June 25, 2001(!) that applicants invention was free of the art, that patentable subject matter existed, and that they would assist us in complying with the various formal requirements to achieve suitable language. After complying with each request, however, yet another new and different and unexpected rejection has been made.

(1) Whether claims 12, 14, 17, 18, and 29-39 are definite under 35 U.S.C. 112, second paragraph.

Claims 12, 14, 17-18, and 29-39 have been rejected under 35 U.S.C. 112, second paragraph, for indefiniteness in the use of the word "component." The rejection further states that substituting "agent" for "component" would overcome this rejection.

From the outset of the examination of this application, Applicants have attempted to streamline the prosecution to eliminate any controversial or contentious issues, as is sometimes required of start-up biotechnology companies. Therefore, in the unentered amendment filed June 20, 2002, Claim 12 was amended as suggested in the Office Action, changing the second "component" to second "agent." Applicants believe the substitution of the word agent for component does not affect the scope or change the meaning of the claim.

(2) Whether claims 12, 14, 17, 18, and 29-39 are enabled under 35 U.S.C. 112, first paragraph.

Claims 12-14, 17-21, and 29-39 have been rejected under 35 U.S.C. 112, first paragraph, for lack of enablement. Before addressing the specific points of the rejection, Applicants seek a point of clarification. Claims 13 and 19-21 were canceled in the response filed March 11, 2002, and because the Office Action indicates that the previous amendment was entered, the list of claims under this rejection cannot be correct. Accordingly, Applicant's argument as follows is restricted to claims 12, 14, 17-18, and 29-39.

The Office Action states that it is "not clear how the recited method allows the second component to bind to the binding agent."

First, Appellants are not clear why this is an enablement rejection, and secondly, the Examiner is required to provide reasons why Appellants' claim language fails to be enabling in this regard. It is the Examiner's initial burden, and because no reasonable explanation is present in the office action, it is respectfully suggested that a prima facie rejection under 35 U.S.C. 112 can not be sustained.

Thirdly, the elements of the claim of concern to the Examiner are all the well known structural elements for binding the binding agent to the second agent. None of them in and of themselves are novel, nor are Appellants claiming them as such. The elements and their

use are thoroughly described in the present specification, at, for example: claim 1; claim 18; claims 33-39; page 13, lines 11+; page 20, lines 8-11; Example 4; Example 7; Example 8, and the Rule 132 Affidavit filed 11/2/01, among many other places throughout the specification and claims as originally filed. Furthermore, the specific types of linkages are extremely well known in the art, structurally and functionally.

As such, it is clear that the claim language is enabled by the specification, because "the requirement is satisfied if, given what they already know, the specification teaches those in the art enough that they can make and use the invention without 'undue experimentation.'" Amgen, Inc. v. Hoeschst Marion Rousell, Inc., 314 F.3d 1313, 1330; 65 USPQ 2d 1385, (Fed. Cir., 2003).

In Appellants' case, the claims as filed, the specification, and examples all teach this claim element, one which is well know to those of ordinary skill in the art.

The Office Action makes this same rejection against the combination of claims 12, 14 and 33. For the reasons noted above, Appellants argue that the Examiner has not satisfied the initial burden required to sustain an enablement rejection under 35 U.S.C. 112.

The Office Action makes this same rejection against the combination of claims 12, 17 and 36. For the reasons noted above, Appellants argue that the Examiner has not satisfied the initial burden required to sustain an enablement rejection under 35 U.S.C. 112.

The Office Action makes this same rejection against the combination of claims 12 and 18. For the reasons noted above, Appellants argue that the Examiner has not satisfied the initial burden required to sustain an enablement rejection under 35 U.S.C. 112.

The Office Action makes this same rejection against the combination of claims 12, and 29-32. For the reasons noted above, Appellants argue that the Examiner has not satisfied the initial burden required to sustain an enablement rejection under 35 U.S.C. 112.

The Office Action makes this same rejection against the combination of claims 12 and 34. For the reasons noted above, Appellants argue that the Examiner has not satisfied the initial burden required to sustain an enablement rejection under 35 U.S.C. 112.

The Office Action makes this same rejection against the combination of claims 12, 34 and 35. For the reasons noted above, Appellants argue that the Examiner has not satisfied the initial burden required to sustain an enablement rejection under 35 U.S.C. 112.

The Office Action makes this same rejection against the combination of claims 12,

34 and 37. For the reasons noted above, Appellants argue that the Examiner has not satisfied the initial burden required to sustain an enablement rejection under 35 U.S.C. 112.

The Office Action makes this same rejection against the combination of claims 12, 34, 37, and 38. For the reasons noted above, Appellants argue that the Examiner has not satisfied the initial burden required to sustain an enablement rejection under 35 U.S.C. 112.

Appellants respectfully but forcefully contend that one of ordinary skill in the art , reviewing the claims and specification as originally filed, are easily enabled to make and use the invention. Further, Applicants respectfully but forcefully contend that the Examiner's initial burden for sustaining this rejection has not been met.

(3) Whether claims 12, 14, 17, 18, and 29-39 were in possession of the inventors under 35 U.S.C. 112, first paragraph.

Claims 12-14, 17-21, and 29-39 have been rejected under 35 U.S.C. 112, first paragraph, as failing to convey to one of ordinary skill in the art that the inventors had possession of the claimed invention (a "written description rejection"). Since claims 13 and 19-21 were canceled in the previous response as noted above, it is believed that the intended claim grouping is claims 12, 14, 17-18, and 29-39, and Appellants' response as follows is restricted to those claims.

Similar to the issue raised above, the Examiner is required to provide reasons why Appellants' claim language fails to comply with the written description requirement. It is the Examiner's initial burden, and because no reasonable explanation is present in the office action, it is respectfully suggested that a prima facie rejection under 35 U.S.C. 112 can not be sustained.

The Examiner, both in this rejection and orally, has required that Appellants' to limit their claimed invention to "one specific combination." However, The Examiner has not provided any support or reasoning why Appellants must do so.

Also, the elements of the claim of concern to the Examiner are all the well known and conventional ligands, anti-ligands, and binding agents. None of them in and of themselves are novel, nor are Appellants claiming them as such. The elements and their use are thoroughly described in the present specification, at, for example: claim 1; claim 18; claims

33-39; page 13, lines 11+; page 20, lines 8-11; Example 4; Example 7; Example 8, and the Rule 132 Affidavit filed 11/2/01, among many other places throughout the specification and claims as originally filed. Furthermore, the specific types of linkages are extremely well known in the art, structurally and functionally.

To sustain a written description rejection, the Office Action must show that the claimed subject matter is not adequately described by the specification. Here, Applicants' specification is replete with both broad and specific examples of ligands, anti-ligands, and binding agents encompassed by the claims, and these elements of the claims are extremely well known to those of ordinary skill in the art. Applicants concede that there are many combinations that would be effective in performing Applicants' claimed invention. But Applicants are not obligated to teach that which is already known, nor are they obligated to disclose each and every possible combination. For example, the ligand, anti-ligand, and binding agent, alone and in combination, are described at page 13, lines 11+; page 20, lines 8-11; Example 4; Example 7; and Example 8, among many other places throughout the specification and claims as originally filed.

Finally, Appellants' specification and Rule 132 affidavit provide concrete, existing examples of the existence of the claimed invention. These are not prophetic examples, but actual laboratory results. It is respectfully and forcefully urged that the Examiner must indicate with reasonable arguments why Applicants were not in possession of the claimed invention.

(4) Other informality and procedural considerations.

Appellants wish to note that they have complied with every request made by the Examiner, indicating in several of their responses that they have filed a continuation application to address more problematic issues raised by the wording of Appellants' claims. Every time Appellants amended the claims in accordance with the guidance of the Examiner, they received a new ground of rejection. For example, the Advisory Action states: "proposed newly amended claim 12 would overcome all of the outstanding rejections. However, a new enablement rejection would be applied ...." This comment is

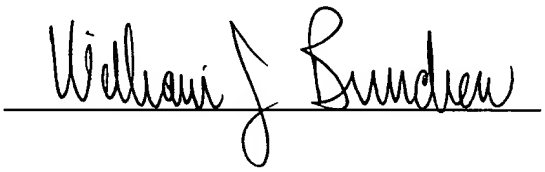
intended merely as a plea for assistance in developing acceptable claims in an application that was indicated by the examiner as being free of the art and "patentable" during our June 2001 interview.

VII. Conclusion

For the reasons noted above, Appellants respectfully contend that each claim is patentable. Therefore, reversal of all rejections is courteously solicited.

Respectfully submitted,

CAHN & SAMUELS, LLP

By: 

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APPENDIX OF CLAIMS ON APPEAL

12 (thrice amended). A method of inducing a thrombus in vivo comprising:

administering a binding agent having a first component for binding the binding agent to a pre-selected site;

administering a second component, said second component specifically binds platelets, and allowing the second component to bind to the binding agent;

binding platelets on the second component;

inducing activation of the platelets; and thereby

allowing a thrombus to form.

14 (amended). The method of claim 12 wherein the binding agent is one or more binding agents selected from the group consisting of an antibody, and fragments or parts thereof.

17 (thrice amended). The method of claim 12 wherein the second component comprises von Willebrand factor.

18 (thrice amended). The method of claim 12 wherein the first component, the second component, or both, further comprise a moiety selected from one or more of the following: biotin, homophyllic peptides and human Fc fragments.

33. The method of claim 14 wherein the binding agent further comprises a biotin ligand.

34. The method of claim 12 wherein allowing the second component to bind to the binding agent comprises administering an anti-ligand that specifically binds the binding agent.

35. The method of claim 34 wherein the anti-ligand is an anti-ligand selected from the group consisting of avidin, streptavidin, neutravidin, and derivatives and analogs thereof

36. The method of claim 17 wherein the second component is von Willebrand factor conjugated with a ligand.

37. The method of claim 34 wherein the second component is von Willebrand factor conjugated with a ligand.

38. The method of claim 37 wherein the second component is conjugated to biotin.

39. The method of claim 12 wherein the binding agent binds to a ligand/receptor complex comprising VEGF/VEGF receptor.